

cross-linking freeze drying, using an organic co-solvent or a solvent system containing a substantially reduced concentration of water for the drying and cross-linking, subjecting the fibre lay and constrained hydrogel to hydrostatic pressure or compressive loading before and during the cross-linking reaction and adding or removing salts and/or controlling the pH to reduce the swelling of the hydrogel before and during cross-linking.

[0132] Also, the fibre lay may be pre-stressed by winding almost all of it in a taught state while applying layers of partially hydrated hydrogel as described above before cross-linking using a chemical agent or irradiation or electrical discharge or photopolymerisation.

[0133] A taughly wound fibre lay containing, in a substantially dehydrated state, either the hydrogel or monomers for forming the hydrogel may be cross-linked with a concentrated solution of glutaraldehyde and/or formaldehyde also comprising polyvinylpyrrolidone or polyethyleneglycol.

[0134] A hydrogel may be given different properties in different parts of the device by applying the component or components for forming the hydrogel in successive layers or regions receiving different treatments.

[0135] In addition to forming a hydrogel within the fibre lay, the component or components for forming the hydrogel may be applied to form a coating to the fibre lay.

[0136] The open porosity of all or part of the device allows for infiltration in vitro or in vivo of living stem cells into the pores of the device. A patient's own living stem cells or those from a donor may be allowed to enter the pores of the device before implantation. Implants infiltrated with stem cells may be immediately implanted or kept in vitro under conditions known to enhance the formation of hyaline or fibrocartilage. In either case, this provides the implant with cells for subsequent formation of living cartilage. Alternatively a patient's own mesenchymal stem cells may be introduced into the porous hydrogel after implantation. However incorporation of cells before implantation may enhance the rate of synthesis of new functional tissues, and in particular, the rate at which a fully functional anchorage of the device into bone is produced.

[0137] Both the porous hydrogel and the fibre component of the fibre lay of the one or more extensions or surfaces may be mineralised with the bone mineral hydroxyapatite thereby producing a material that substantially mimics bone in its physical properties, is osteoconductive and osteoinductive, is biocompatible and serves as an attachment site for mesenchymal cells and in these ways facilitates the attachment and integration of the device to the underlying bone.

[0138] The silk fibroin solution in the hydrogel may first be gelled with a weakly acidic solution containing phosphate ions and, after freezing to create a porous matrix, the material may be treated with a solution containing calcium ions to form hydroxyapatite. Alternatively hydroxyapatite may be deposited in the fibre lay and porous hydrogel after cross-linking by repeated alternating dippings for 1 hour in 120 mM disodium hydrogen phosphate at pH 7, followed by 1 hour in 200 mM calcium chloride solution at pH 7.4 all at 20 degrees C. A further alternative is to treat fibre lay and enclosed hydrogel with simulated body fluid. In this case citric acid may be added to act as a nucleating agent at the surface.

[0139] One or more extensions to the device may be mineralised by the extension being immersed in the mineralising solutions described in protocol C without mineralising the remainder of the device. Where it is desired to mineralise one

or more surfaces or outer layers of the device the surface may be immersed or otherwise treated with a thin layer of the mineralizing solutions.

[0140] A thin waterproof biocompatible membrane may be incorporated into the device during the preparation of the fibre lay to limit the spread of mineralising solutions to the desired surface or surfaces.

[0141] A layer or layers or extensions may be prepared separately and subsequently mineralized before being stitched or otherwise attached to non-mineralised component or components of the device. The mineralised hydrogel may be used on its own as a material for the repair of bone or the fixation of orthopaedic devices (e.g. endoprostheses) in bone.

[0142] The device is intended for the repair of defects in articular cartilage or the partial or complete replacement of one or both menisci of the knee or the temporomandibular meniscus or the replacement of one or more intervertebral discs.

1. An implantable cartilaginous tissue repair device comprising:

a biocompatible and at least partially bioresorbable three-dimensional fibre lay

at least partially infiltrated by

a biocompatible and at least partially bioresorbable, substantially porous hydrogel

whereby, in use, cells are contained within at least some of the pores of the device.

2. An implantable cartilaginous tissue repair device according to claim 1 in which said three-dimensional fibre lay is substantially biomimetic of the fibre pattern of a cartilaginous tissue which is to be repaired.

3. An implantable cartilaginous tissue repair device according to claim 1 in which the fibres of said three-dimensional fibre lay comprise of fibres selected from the group of fibres consisting of: natural mulberry-silk fibres or natural wild-silk fibres or spider-silk fibres or fibres of a recombinant protein based substantially on the proteins of mulberry silk or fibres of a recombinant protein based substantially on the proteins of wild silk or fibres of a recombinant protein based substantially on the proteins of spider silk.

4. An implantable cartilaginous tissue repair device according to claim 1 in which said substantially porous hydrogel comprises at least one component selected from the group of components consisting of: regenerated silk fibroin from mulberry silk or regenerated silk fibroin from wild silk or regenerated spidroin from spider silk or gelatin or fibrin or fibronectin or an alginate or hyaluronic acid or chondroitin sulphate.

5. An implantable cartilaginous tissue repair device according to claim 1 in which the average pore diameter is between 50 μm and 300 μm .

6. An implantable cartilaginous tissue repair device according to claim 1 further comprises:

one or more covalently bound growth factors selected from the list of growth factors consisting of: Beta-FGF or TGF-beta 1 or GDF-5 or insulin-like growth factor or basic fibroblast growth factor or cartilage tissue growth factor or osteogenic protein-1

whereby, the binding and/or differentiation of mesenchymal or stem cells is stimulated in order to either form cartilage or to stimulate proteoglycan secretion.

7. An implantable cartilaginous tissue repair device according to claim 1 further comprises: repair device claims which further comprises:

an integral attachment means for attaching said three-dimensional fibre lay and/or said porous hydrogel to bone.